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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,581	01/17/2006	Thomas Link	23062	7537

151 7590 12/18/2009

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PATENT LAW DEPARTMENT
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EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
12/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,581	LINK ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/24/09 has been entered.

Response to Amendments

Applicant's amendments filed 9/24/09 to the claims have been entered. Claims 16-20 and 22-27 have been canceled in this reply. Claims 28 and 29 have been added. Claims 28 and 29 remain pending in the current application, both of which are being considered on their merits. References not included with this Office action can be found in a prior action. Any rejections of record not particularly addressed below are withdrawn in light of the claim amendments and applicant's comments.

Applicant is encouraged to review the provisions of 37 C.F.R. 1.121(c) regarding status identifiers for amended claims. The proper identifier for new claims is "new." Because the status of the claims is accurate and clear (see M.P.E.P. § 714(C), subsection E), the examiner elects not to hold the instant reply as noncompliant. Future replies using unacceptable status identifiers will be considered nonresponsive.

Election/Restrictions

Applicant's election with traverse of the species “CHO cells” and “immunoglobulins” in the reply filed on 5/13/08 is still in effect over the claims. The amendments to the claims fall within the scope of these elections.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The language of a claim must make it clear what subject matter the claim encompasses to adequately delineate its "metes and bounds.” See, e.g., *In re Hammack*, 427 F 2d. 1378, 1382, 166 USPQ 204, 208 (CCPA 1970); *In re Venezia* 530 F 2d. 956, 958, 189 USPQ 149, 151 (CCPA 1976); *In re Goffe*, 526 F 2d. 1393, 1397, 188 USPQ 131, 135 (CCPA 1975); *In re Watson*, 517 F 2d. 465, 477, 186 USPQ 11, 20 (CCPA 1975); and *In re Knowlton,* 481 F 2d. 1357, 1366, 178 USPQ 486, 492 (CCPA 1973). The courts have also indicated that before claimed subject matter can properly be compared to the prior art, it is essential to know what the claims do in fact cover. See, e.g., *In re Steele*, 305 F 2d. 859, 134 USPQ 292 (CCPA 1962); *In re Moore*, 439 F 2d. 1232, 169 USPQ 236 (CCPA 1969); and *In re Merat*, 519 F 2d. 1390, 186 USPQ 471 (CCPA 1975). In this case, the claims are so indefinite as to preclude a substantive search by the examiner.

Claim 28 allows culturing a CHO cell in "ProCHO4-CDM medium," which appears to refer to a trade name for a medium produced by the BioWhittaker corporation (see reference U). M.P.E.P. § 2173.05(u) recites, "It is important to recognize that a trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus a trademark or trade name does not identify or describe the goods associated with the trademark or trade name." If the trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. § 112, second paragraph. *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). Such is the case here. Neither the specification nor the manufacturer's website provides a description of the ProCHO4-CDM medium such that the skilled artisan could practice the claimed method if the manufacturer ceased its production. Clarification is required. The claim must be amended to remove the trade name if applicant cannot provide a list of all of the components of ProCHO4-CDM medium; the description on the manufacturer's website, which only indicates a few components that are not present in the medium, is insufficient to describe it.

Claim 28 allows culturing a CHO cell in "DMEM/Ham's F-12 medium," which is confusing because it is not clear whether this limitation allows culturing the cell in either DMEM or F-12 medium or in some mixture of the two. Clarification is required.

Claim 28 requires feeding glucose "when the viable cell count is $1.8*10^6$ cells/ml or more," but it is not clear to which volume the "cells/ml" limitation refers. Clarification is required.

Claim 28 requires feeding glucose at "a constant glucose concentration," but it is not clear whether this concentration refers to the concentration of glucose in the solution being fed or the concentration of glucose in the culture once it has been added. Clarification is required.

Claim 28 requires that the constant flow rate is "from D=0.03/h to D=0.05/h," which is wholly confusing. It is not clear what the variable "D" refers to, and no units are provided for the values 0.03 and 0.05. Clarification is required.

Applicant's arguments regarding the withdrawn rejections of record have been considered as they pertain to these new grounds of rejection, but they are not persuasive. Applicant is urged to review 37 C.F.R. 1.111(b), which requires that a reply both distinctly and specifically point out the supposed errors in the examiner's action and reply to every ground of objection and rejection in the prior Office action. The reply must present arguments pointing out the specific distinctions believed to render the claims, **including any newly presented claims,** patentable over any applied references. The arguments submitted with the instant reply do not fully comply with 37 C.F.R. 1.111(b) because they do not particularly address the limitations of the new claims with respect to the withdrawn rejections, but in the interest of compact prosecution, the examiner declined to send a notice of noncompliance at this time. If future replies include mere allegations of patentability such as those at pages 4-5 of the reply and not particular arguments that compare the claim limitations to the cited references, however, they will be considered noncompliant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Folena-Wasserman et al. (1993, U.S. Patent 5,252,216; reference A) taken in view of Keen et al. (1994, U.S. Patent 5,316,938; reference B). In the interest of compact prosecution, the claims are interpreted as being drawn to a method for producing an antibody comprising culturing CHO cells in a medium at a pH between 6.7 and 7.7; measuring the viable cell count; feeding glucose at some constant rate when the cell count reaches $1.8x10^6$ cells/mL medium or more; and recovering the antibody produced by the CHO cells. In some dependent claims, the concentration of glucose in the medium is maintained at about 24mmol/L, i.e. 4.3g/L.

Folena-Wasserman teaches a method for producing a recombinant protein comprising culturing CHO cells in a mixture of DMEM and Ham's F-12 medium until the cells reach a critical concentration, then perfusing glucose into the culture at a constant rate such that the glucose concentration within the culture remains at 1.0g/L (i.e., 6 mmol/L, which is "about 24 mmol/L"), and then recovering the recombinant protein. See column 11, line 41, through column 12, line 46. Folena-Wasserman teaches that the method may be used to produce virtually any recombinant protein. See column 12, lines 47-58.

Folena-Wasserman does not specifically teach producing antibodies. Folena-Wasserman does not exemplify an embodiment in which glucose is added once the cell count reaches $1.8x10^6$ cells/mL medium or one in which the glucose level is higher than 1.0 g/L (6 mmol/L).

Keen teaches a method for producing Campath 1H human IgG antibody from recombinant CHO cells comprising culturing the cells in serum-free WCM4 medium, which contains 4.5g glucose/L (25 mmol/L), at pH 6.5-7.5 and recovering the secreted antibody. See example 3 at column 8; Table 1 at columns 4-5; and column 3, lines 30-40. Keen teaches that the medium can support cells at a density up to or greater than $1.5x10^6$ cells/mL. See column 6, lines 44-55, and line 38 of Table 3 at column 11. Keen teaches that any antibody can be produced using the medium. See column 6, line 56 et seq.

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the recombinant cells and medium of Keen for the cells and

medium of Folena-Wasserman in the method of Folena-Wasserman because the cited references establish that both are useful for producing recombinant proteins. The skilled artisan would have been motivated to make this substitution in order to yield antibodies, which are therapeutically useful.

The selection of the concentration of cells in the medium at the time of glucose addition would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Folena-Wasserman teaches waiting to add glucose until the cell density reaches a critical point and that Keen's medium can support growth of cells at the claimed high density. A holding of obviousness over the cited claims is therefore clearly required.

The selection of the concentration of glucose in the medium would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Folena-Wasserman and Keen teach that CHO cells produce recombinant proteins at 1.0-4.5g glucose/L (i.e., 6-25 mmol/L). A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Folena-Wasserman to use the antibody-producing cells, medium, high glucose concentration, and high cell density of Keen in order to produce antibodies because Folena-Wasserman's method produces high levels of recombinant protein and Keen's system produces high levels of antibodies specifically.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Applicant's arguments regarding the withdrawn rejections of record have been considered as they pertain to this new ground of rejection, but they are not persuasive. Applicant is urged to review 37 C.F.R. 1.111(b), which requires that a reply both distinctly and specifically point out the supposed errors in the examiner's action and reply to every ground of objection and rejection in the prior Office action. The reply must present arguments pointing out the specific distinctions believed to render the claims, **including any newly presented claims,** patentable over any applied references. The arguments submitted with the instant reply do not fully comply with 37 C.F.R. 1.111(b) because they do not particularly address the limitations of the new claims with respect to the withdrawn rejections, but in the interest of compact prosecution, the examiner declined to send a notice of noncompliance at this time. If future replies include mere allegations of patentability such as those at pages 4-5 of the reply and not particular arguments that compare the claim limitations to the cited references, however, they will be considered noncompliant.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art

may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651